

ORIGINAL



# Lung ultrasound allows the diagnosis of weaning-induced pulmonary oedema

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## Abstract

**Rationale:** Detecting weaning-induced pulmonary oedema (WIPO) is important because its treatment might prompt extubation. For this purpose, lung ultrasound might be an attractive tool, since it demonstrates pulmonary oedema through the appearance of B-lines.

**Objectives:** To test the ideal profile (increase in the number of B-lines) for diagnosing WIPO.

**Methods:** Before and at the end of 62 spontaneous breathing trials (SBT) performed in 42 patients, we prospectively assessed lung ultrasound on four anterior chest wall points. B-lines were counted before and at the end of SBT. We looked for the threshold of B-line increase (Delta-B-lines) that provided the best diagnostic accuracy, compared to the reference diagnosis of WIPO established by experts blinded to lung ultrasound.

**Results:** SBT failed in 33 cases. WIPO occurred in 17 cases and all failed. The best diagnostic accuracy was reached with a Delta-B-lines  $\geq 6$ . Among WIPO, the number of B-lines increased by  $\geq 6$  in 15 cases (including 13 cases with an increase of  $\geq 8$  B-lines). Among the 16 cases with SBT failure but without WIPO, the Delta-B-lines was  $\geq 6$  in two cases. Among the 33 cases with SBT failure, this profile diagnosed WIPO with a sensitivity of 88% (64–98) and a specificity of 88% (62–98) [area under the receiver operating characteristic curve 0.91 (0.75–0.98)]. Among the 29 cases with SBT success, a Delta-B-lines  $\geq 6$  occurred in two cases.

**Conclusions:** This study suggests that a Delta-B-lines  $\geq 6$  on four anterior points allows the diagnosis of WIPO with the best accuracy. This should be confirmed in larger populations.

**Keywords:** Heart failure, Interstitial oedema, Heart–lung interactions, Extravascular lung water, Mechanical ventilation

## Introduction

Failure of weaning from mechanical ventilation is independently associated with poor outcome in critically ill patients [1]. Identifying the cause of weaning failure helps determine the appropriate treatment, which may prompt weaning [2, 3]. Weaning-induced pulmonary

oedema (WIPO) is a common cause of weaning failure. During weaning from mechanical ventilation, usually during a spontaneous breathing trial (SBT), heart–lung interactions impair the cardiac loading conditions, which may lead to pulmonary oedema. Detecting WIPO is potentially important and useful, because it can be easily treated [4, 5].

Measuring the pulmonary artery occlusion pressure during an SBT directly evidences the increase in hydrostatic pulmonary pressure [3]. However, less invasive alternative methods have been developed, like the assessment of blood volume contraction [6, 7], increase

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in B-type natriuretic peptide (BNP) [7, 8], in the left ventricular filling pressure at echocardiography [9] or in extravascular lung water [7].

Lung ultrasound in critically ill patients (LUCI) may be an alternative. By detecting multiple B-lines that allows the diagnosis of interstitial syndrome, lung ultrasound accurately detects pulmonary oedema, including from haemodynamic origin [10–12]. B-lines have been correlated with NT-pro-BNP in breathless patients [13, 14] and with extravascular lung water accumulation [15]. Nevertheless, LUCI has never been tested as a diagnostic tool to detect WIPO.

In the present study, our hypothesis was that it is possible to determine an increase in the number of B-lines that allows the diagnosis of WIPO. Our goal was to determine this threshold of B-line increase (Delta-B-lines) that reliably detected WIPO, first in patients failing an SBT, because the question of WIPO mainly arises in such patients, and second in the general population of patients performing an SBT.

## Patients and methods

### Patients

This study was performed in the medical intensive care unit of a university hospital between May 2015 and September 2015. As approved by the institutional review board of our institution (Comité Pour la Protection des Personnes Ile-de-France 7, ID2011A0170140), all patients were informed about the study and agreed to participate. Patients were consecutively included according to the following criteria: (1) invasive mechanical ventilation, (2) a planned SBT on a T tube, according to the decision of clinicians in charge. They screened patients for SBT according to current guidelines [16] and (3) investigators' availability. Exclusion criteria were (1) age less than 18 years, (2) pregnancy and (3) poor cardiac echogenicity (impossibility to analyse the mitral inflow).

### Management of the SBT

SBT was performed on a T piece [17]. Poor tolerance of SBT was defined as previously described [18] (Supplemental Material). The decision to stop SBT was made by physicians. The duration of the SBT was 60 min, or longer in patients with neurologic deficit.

Patients who successfully passed the SBT were extubated and followed up for 48 h. Weaning failure was diagnosed if SBT was interrupted because of clinical intolerance or if the patient was extubated but needed mechanical ventilation (invasive or non-invasive) or died within the following 48 h.

## Take-home message

Weaning from mechanical ventilation may induce weaning-induced pulmonary oedema (WIPO). We report that lung ultrasound was able to detect the occurrence of WIPO, by showing that a value of 6 in the increase of B-lines on four anterior points of the chest wall provides the best accuracy.

## Haemodynamic and biological variables

Before and at the end of SBT (at 60 min in case of SBT success, earlier in case of SBT failure), we recorded:

1. Clinical variables: respiratory rate, pulse oxygen saturation, heart rate and arterial pressure.
2. Biological variables: arterial blood gas analysis, haemoglobin concentration (ABL 800flex device, Radiometer, Copenhagen, Denmark) and concentration of total plasma proteins (Modular P device, Roche diagnostics, Basel, Switzerland).

## Echocardiographic variables

Echocardiographic variables were measured before and at the end of SBT using a CX50 ultrasound device with a S5–1 MHz probe (Philips Healthcare, DA Best, the Netherlands). The left ventricular ejection fraction was assessed by the monoplane Simpson method. The left ventricular diastolic function was assessed by measuring velocities of the mitral E and A waves and of the e' wave of the external mitral annulus and by calculating the E/e' ratio.

## Lung ultrasound

Before and at the end of SBT, using the CX-50 device with a C8–5 MHz microconvex probe, one of two investigators (AE, MG) acquired lung ultrasound images. The LUCI analysis is derived from the methodology of the BLUE protocol [12, 19, 20]. The number of B-lines was counted in a rib short-axis scan between two ribs at the four standardised BLUE points [19] or, if a lung consolidation was present, at the nearest alternative point, in order to favour the B-line counting ("flexible" BLUE points, see Supplemental Material). Care was taken to apply the probe at the same precise area. The average duration of a test is less than 2 min. Images were stored and the increase in the number of B-lines (Delta-B-lines) was analysed a posteriori by two experts in lung ultrasound blinded to patient diagnosis (DL, GM) (Fig. 1).

## Reference diagnosis of WIPO

As in previous studies [21–23], the reference diagnosis of WIPO was established a posteriori by two experts (JLT and XM) blinded to LUCI data on criteria listed in

Supplemental Table E1. Cases were excluded from analysis in case of no diagnostic agreement between the experts.

#### Data analysis

The principle of data analysis was to determine the threshold of B-line increase that allows the diagnosis of WIPO with the best accuracy. The primary analysis was performed in the subgroup of patients who failed SBT, because it is in these patients that the question of WIPO mainly arises. In this analysis, the subgroup of patients with SBT success and extubation success was used as a control group, in which the number of B-lines should not change if LUCI was reliable to detect WIPO. The secondary analysis was performed in the whole population of patients undergoing SBT. In patients who performed several SBT, all episodes were included in primary and secondary analyses. The same analyses were also performed by considering only the first SBT of these patients.

#### Statistical analysis

Data are expressed as number (percentage of the whole population), means  $\pm$  SD, mean [95% confidence interval (CI)] or median [interquartile range]. Comparisons between cases with versus cases without WIPO were assessed by a two-tailed Student's *t* test, a  $\chi^2$  test or a Mann–Whitney *U* test, depending on data distribution (Kolmogorov–Smirnov test). Comparisons between before versus at the end of SBT were assessed by a paired Student's *t* test or a Wilcoxon signed rank sum test, depending on data distribution.

The Delta-B-lines was compared with the reference diagnosis of WIPO (referred to as “WIPO” in the text) and a receiver operating characteristic (ROC) curve was constructed, varying the diagnostic threshold. Sensitivity was calculated as the proportion of true positives among cases with WIPO, and specificity as the proportion of true negatives among cases without WIPO. Positive predictive value was calculated as the proportion of true positives among cases with a B-lines increase higher than the chosen cut-off, and negative predictive value as the proportion of false negatives among cases with a B-lines increase lower than the chosen cut-off. The best diagnostic threshold was defined as the one providing the lowest Youden index (sensitivity + specificity – 1).

Making the hypothesis that WIPO was going to induce an increase in extravascular lung water by  $4 \pm 4$  mL/kg [7], based on the relationship between the amount of lung water and the number of B-lines [15], expecting a number of B-lines at baseline of  $4 \pm 4$ , and taking into account an  $\alpha$  risk of 5% and a  $\beta$  risk of 10%, we planned to include 68 SBT. The statistical analysis was performed with the MedCalc 11.6.0 software (MedCalc, Mariakerke, Belgium).

## Results

#### Patient characteristics.

The 43 included patients performed 64 SBT (“cases” below). One case was excluded because of inconclusive diagnosis and one because of local interferences impeding obtention of lung ultrasound images of sufficient quality. There was no significant difference in baseline characteristics between patients with at least one episode of WIPO and the other ones (Table 1).

#### Issue of SBT

Among the 62 SBT that were analysed (in 42 patients), 33 failed (Fig. E1). Seventeen WIPO occurred, i.e. the prevalence of WIPO was 27% of all SBT and 52% of failing SBT. All cases of WIPO led to SBT failure and all occurred during the SBT. In 16 cases, the SBT failed without WIPO. Among these cases, the reason given for SBT failure was respiratory exhaustion with hypoxemia in ten cases and consequences of neurological disorder (ICU-acquired weakness, myasthenia) in six other cases (Fig. E1). Since they were included in the definition of WIPO, plasma protein and haemoglobin concentrations and the E/e' ratio increased during SBT significantly only in cases with WIPO (Table 2).

#### Characteristics of lung ultrasound before SBT

Before the SBT, the average number of total B-lines was  $5 \pm 5$  in cases with WIPO and  $3 \pm 3$  in cases without WIPO ( $p = 0.01$ ) (Supplemental Table E2). Lung consolidations at the BLUE points were previously present in 10 of 248 quadrants (inviting investigators to move the probe elsewhere).

#### Threshold value of Delta-B-lines to diagnose WIPO

In the primary analysis, among the 33 cases associated with SBT failure, the best accuracy for diagnosing WIPO was reached when the Delta-B-lines was  $\geq 6$ . In these cases, a Delta-B-lines  $\geq 6$  allowed the diagnosis of WIPO with a sensitivity of 88% (95% CI 64–98), a specificity of 88% (95% CI 62–98), a positive predictive value of 82% (95% CI 67–97) and a negative predictive value of 88% (95% CI 65–96) (Fig. 1, Table 3). The area under the ROC curve was 0.91 (95% CI 0.75–0.98) (Supplemental Fig. E2). Among the 17 cases with WIPO, a Delta-B-lines  $\geq 6$  occurred in 15 cases. Among the 16 cases with SBT failure but without WIPO, a Delta-B-lines  $\geq 6$  occurred in two cases (Fig. 2 and Supplemental Table 1). In the 29 cases with SBT success, it occurred in two cases.

When the secondary analysis was performed by considering all the cases and not only those in which the SBT failed, the best accuracy for diagnosing WIPO was reached when the Delta-B-lines was  $\geq 6$ . The sensitivity was 88% (95% CI 64–98), the specificity was 91% (95%

**Table 1 Patient characteristics**

	All patients (n = 42)	Patients who experienced at least one episode of WIPO (n = 11)	Patients who did not experience any episode of WIPO (n = 31)
Age (years, mean ± SD)	62 ± 16	62 ± 15	58 ± 16
Male gender (n, %)	20 (48%)	5 (45%)	15 (48%)
BMI (kg/m <sup>2</sup> , mean ± SD)	22 ± 7	27 ± 8	22 ± 7
<b>Comorbidities</b>			
Cardiovascular comorbidities (n, %)	23 (55%)	8 (73%)	15 (48%)
COPD (n, %)	6 (14%)	3 (27%)	3 (10%)
Chronic renal failure (n, %)	6 (14%)	1 (9%)	5 (16%)
Diabetes mellitus (n, %)	6 (14%)	2 (18%)	4 (13%)
Immunocompromised patients (n, %)	12 (29%)	1 (9%)	11 (35%)
SAPS2 (mean ± SD)	48 ± 19	45 ± 27	49 ± 16
<b>Reason for ICU admission</b>			
Severe pneumonia (n, %)	12 (29%)	4 (36%)	8 (26%)
Septic shock (n, %)	13 (31%)	5 (45%)	8 (26%)
Coma (n, %)	5 (12%)	0	5 (16%)
Other neurological disorders (n, %)	4 (10%)	0	4 (13%)
Cardiac arrest (n, %)	3 (7%)	1 (9%)	2 (6%)
Haemorrhagic shock (n, %)	2 (5%)	0	2 (6%)
Other (n, %)	3 (7%)	1 (9%)	2 (6%)
ICU length of stay (days, mean ± SD)	13 ± 16	16 ± 10	13 ± 17
ICU mortality (n, %)	6 (14%)	3 (27%)	3 (10%)

SAPS simplified acute physiologic score, BMI body mass index, COPD chronic obstructive pulmonary disease, ICU intensive care unit, WIPO weaning-induced pulmonary oedema

Cardiovascular comorbidities include arterial hypertension, arrhythmias and coronary artery diseases

There was no significant difference between patients who experienced at least one episode of WIPO and the other ones

**Table 2 Evolution of variables during the spontaneous breathing trial according to occurrence of weaning-induced pulmonary oedema**

	Cases with WIPO (n = 17)		Cases without WIPO (n = 45)	
	Before SBT	At the end of SBT	Before SBT	At the end of SBT
Heart rate (beats/min, mean ± SD)	91 ± 16	106 ± 24 <sup>#</sup>	92 ± 18	96 ± 15
Mean arterial pressure (mmHg, mean ± SD)	89 ± 15	102 ± 16 <sup>#</sup>	84 ± 17	90 ± 14 <sup>#*</sup>
Respiratory rate (cycles/min, mean ± SD)	21 ± 5	28 ± 7 <sup>#</sup>	20 ± 5	23 ± 7 <sup>#*</sup>
pH (mean ± SD)	7.43 ± 0.06	7.35 ± 0.11 <sup>#</sup>	7.43 ± 0.05	7.41 ± 0.06 <sup>#*</sup>
PaO <sub>2</sub> (mmHg, mean ± SD)	93 ± 17	72 ± 12 <sup>#</sup>	96 ± 18	87 ± 27 <sup>#*</sup>
PaCO <sub>2</sub> (mmHg, mean ± SD)	40 ± 12	51 ± 22 <sup>#</sup>	37 ± 8	39 ± 8 <sup>#*</sup>
SaO <sub>2</sub> (%), mean ± SD)	97 ± 1	92 ± 4 <sup>#</sup>	97 ± 2	95 ± 4 <sup>#*</sup>
<b>Transthoracic echocardiography variables</b>				
Left ventricle ejection fraction (%), mean ± SD)	43 ± 11	–	47 ± 9	–
E/A (mean ± SD)	1.0 ± 0.6	1.3 ± 0.9	1.2 ± 0.6	1.2 ± 0.7
E/e' (mean ± SD)	9.2 ± 3.2	10.6 ± 3.7 <sup>#</sup>	9.1 ± 4.4	9.2 ± 4.3
Haemoglobin blood concentration (g/dL, mean ± SD)	10.2 ± 1.9	11.2 ± 1.7 <sup>#</sup>	9.8 ± 1.7	9.9 ± 1.8 <sup>*</sup>
Plasma protein concentration (g/L, mean ± SD)	52 ± 5	58 ± 7 <sup>#</sup>	59 ± 10 <sup>*</sup>	60 ± 10 <sup>#</sup>

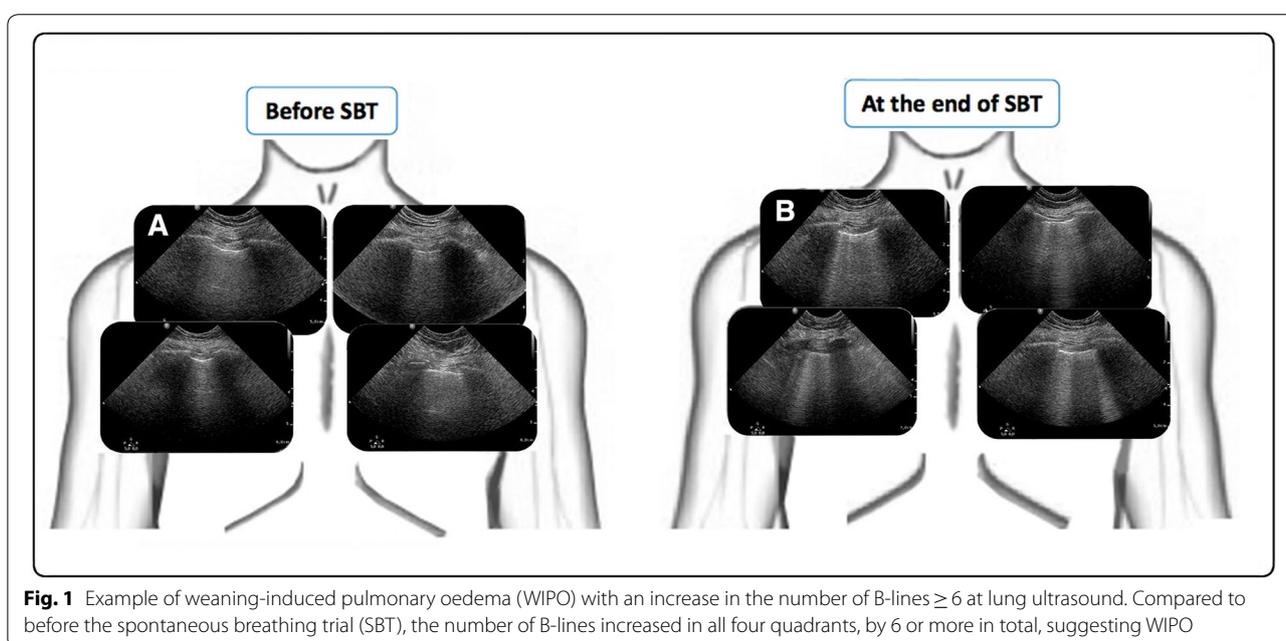
SBT spontaneous breathing trial, PaO<sub>2</sub> arterial oxygen tension, PaCO<sub>2</sub> arterial carbon dioxide tension, SaO<sub>2</sub> arterial oxygen saturation, WIPO weaning-induced pulmonary oedema

<sup>#</sup> p < 0.05 at the end of SBT vs. before SBT; <sup>\*</sup>p < 0.05 cases without WIPO vs. cases with WIPO

**Table 3** Criterion values and features of the ROC curve for the increase in B-lines for establishing the diagnosis of weaning-induced pulmonary oedema in cases in which the spontaneous breathing trial failed

Criterion	Sensitivity	95% CI	Specificity	95% CI	+ LR	95% CI	- LR	95% CI	PPV	95% CI	NPV	95% CI
$\geq 1$	100	80–100	0	0–21	1.00	1.0–1.0			52	52–52		
$\geq 2$	100	80–100	44	20–70	1.78	1.2–2.7	0		65	55–74	100	
$\geq 3$	94	71–100	69	41–89	3.01	1.4–6.3	0.086	0.01–0.6	76	61–87	92	62–99
$\geq 5$	94	71–100	75	48–93	3.76	1.6–8.9	0.078	0.01–0.5	80	63–90	92	64–99
$\geq 6$	88	64–98	88	62–98	7.0	1.9–26.1	0.13	0.04–0.5	82	67–97	88	65–96
$\geq 7$	76	50–93	88	62–98	6.12	1.6–23.0	0.27	0.1–0.6	87	63–96	78	59–89
$\geq 8$	76	50–93	94	70–100	12.24	1.8–83.1	0.25	0.1–0.6	93	66–99	79	61–90
$\geq 12$	12	2–36	94	70–100	1.88	0.2–18.8	0.94	0.8–1.2	67	17–95	50	45–55
$\geq 13$	6	0–29	100	79–100			0.94	0.8–1.1	100		50	47–53
$\geq 14$	0	0–20	100	79–100			1	1.0–1.0			49	49–49

CI confidence interval, NPV negative predictive value, PPV positive predictive value, +LR positive likelihood ratio, -LRs negative likelihood ratio



**Fig. 1** Example of weaning-induced pulmonary oedema (WIPO) with an increase in the number of B-lines  $\geq 6$  at lung ultrasound. Compared to before the spontaneous breathing trial (SBT), the number of B-lines increased in all four quadrants, by 6 or more in total, suggesting WIPO

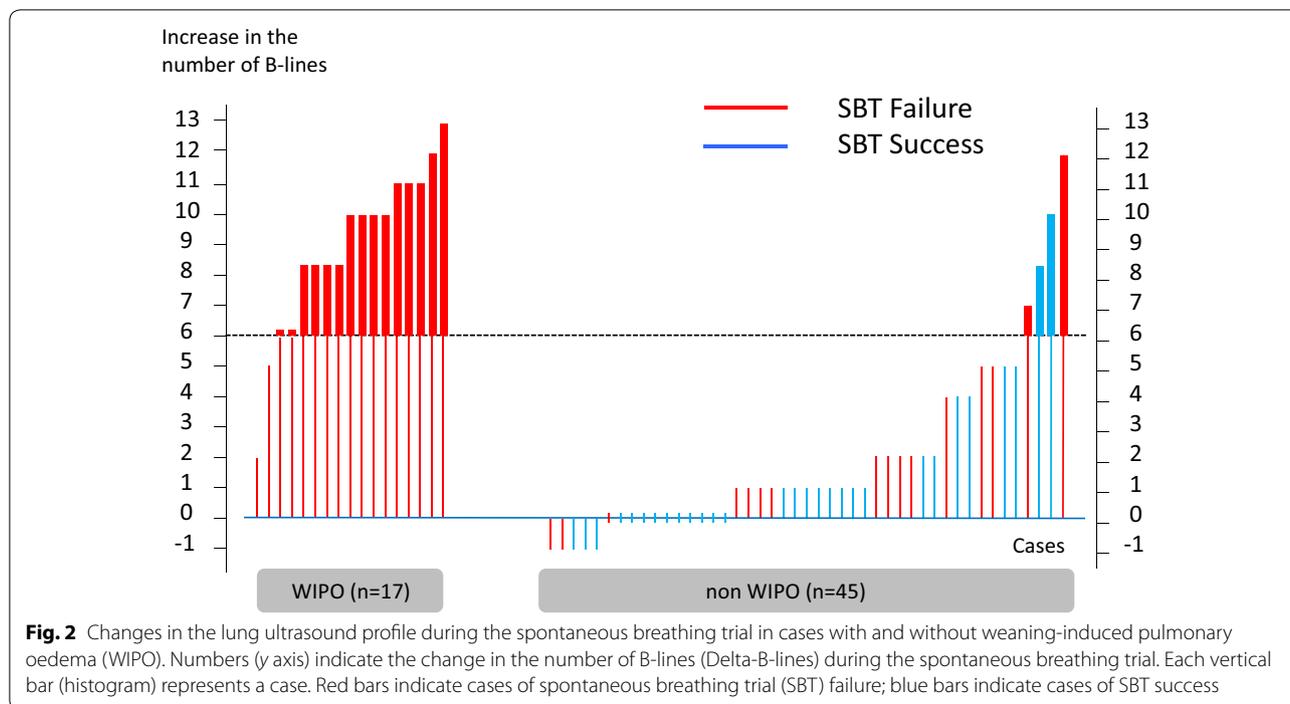
CI 79–98), the positive predictive value was 79% (95% CI 59–91) and the negative predictive value was 95% (95% CI 85–99) (Table 3). The area under the ROC curve was 0.89 (95% CI 0.85–0.99).

When considering only one SBT per patient, in patients in whom the SBT failed, the best accuracy to diagnose WIPO was reached, again, when the Delta-B-lines was  $\geq 6$ . It provided a sensitivity of 89% (95% CI 52–100), a specificity of 91% (95% CI 59–100), a positive predictive value of 89% (95% CI 55–98) and a negative predictive value of 91% (95% CI 61–99). The area under the ROC curve was 0.90 (95% CI 0.69–0.99).

## Discussion

Our results suggest that WIPO can be accurately diagnosed if the total number of B-lines counted at four points of the anterior chest increases by more than 6.

In the present study, WIPO occurred in more than a quarter of all SBT. This confirms the high incidence of WIPO already suggested by previous studies [5–7, 22–24], which reported an incidence of 44% [23] to 87% [22] of weaning failures. Since weaning failure is associated with poor outcome [1], a reliable detection of WIPO should prompt the initiation of its treatment, which is often effective [2, 3], and eventually lead to weaning success.



For many years, the reference criterion for diagnosing WIPO was an SBT-induced increase in the pulmonary artery occlusion pressure, measured through a pulmonary artery catheter [3, 4, 25]. Some alternatives have been developed. A significant increase in the B-type natriuretic peptide or the N-terminal B-type natriuretic peptide during the SBT has been shown to be reliable [7, 8, 26]. Another biological method is based on the haemoconcentration that is induced during pulmonary oedema by the filtration of a significant volume of plasma throughout the pulmonary alveolo-capillary barrier [27]. A significant haemoconcentration, as assessed by an increase in the haemoglobin and/or of the plasma protein concentration provides a reliable diagnosis of WIPO [6, 7]. Echocardiography could be useful, since it estimates the left ventricular filling pressure through the Doppler analysis of the mitral inflow and annulus motion [9] even if there may be heterogeneity in diastolic dysfunction echocardiographic criteria during weaning failure [28]. Transpulmonary thermodilution enables one to directly show the increase in extravascular lung water during WIPO [29], but this requires a specific and invasive device [30].

Studies dealing with the use of lung ultrasound in the context of weaning have rather calculated lung ultrasound scores with aeration loss (without specifically addressing the issue of WIPO) [31] or assessed post-extubation distress [32]. Our study specifically focuses on WIPO. Advantages of lung ultrasound for diagnosing WIPO are numerous. It provides a non-invasive and

direct assessment of lung water accumulation. By detecting lung interstitial syndrome (the first stage of haemodynamic pulmonary oedema), LUCI can demonstrate the earliest stage of WIPO. Indeed, interstitial syndrome is diffuse and therefore visible at the anterior chest wall before any clinical or biological signs occur. This is why only four anterior points were used; they have already shown a high accuracy for diagnosing haemodynamic pulmonary oedema [10, 19, 20]. Consequently it was not necessary to scan posterolateral areas, where B-lines are often present, due to previous disorders in critically ill patients, or even gravity in normal subjects [19, 20]. So, the acquisition and analysis can be performed within 2 min, with a real-time assessment of the lung surface modification. LUCI is easier to learn and perform compared to Doppler echocardiography [30, 31, 33]. Lastly, in case of lack of a microconvex probe, the ergonomics of other probes will be perfectly suitable for scanning the easy-to-access anterior wall (see Supplemental Material). Potential limitations are subcutaneous emphysema, rare giant bullous emphysema (which may generate a paucity of B-lines), pre-existing pathologic B-lines (e.g. lung fibrosis) and dressings.

If B-lines appear during an SBT, apart from WIPO, no differential diagnosis can be reasonably discussed to our knowledge (as opposed to the BLUE protocol, where the main differential diagnosis is pneumonia). In this regard, it was not self-evident before performing the study that LUCI could easily allow the diagnosis of WIPO, as it included patients who had been ventilated for several days.

In the present study, the threshold providing the best diagnosis accuracy was an increase of six B-lines, i.e. the theoretical value of 1.5 line (e.g. 1 or 2 lines) per BLUE point. All patients with a Delta-B-lines  $\geq 6$  gained at least one B-line per point. Most of our patients with WIPO had an increase in B-lines far superior to 6 (13 with a Delta-8) (Fig. 2 and Supplemental Table E2). This study may clarify a point: up to now, it was difficult to classify the pattern of two B-lines (referred to as pre-lung rockets). Current knowledge indicates that one B-line can be normal (possibly a fissure), while three B-lines (or more) indicate pulmonary oedema [34]; the present work allows us to make the hypothesis that pre-lung rockets may be an early stage of pulmonary oedema. The rules previously published highlighted the definition of lung rockets (i.e. three B-lines) for diagnosing haemodynamic pulmonary oedema [19, 34]. Yet the present study is a variant of the BLUE protocol. First, the intensivist was present in order to detect the presence of pulmonary oedema at a very early stage, while patients of the BLUE protocol were seen longer after the start of hydrostatic lung oedema. Anatomically, there is space for three subpleural interlobular septa between two ribs. The fluid excess may invade some of them initially (following possible haemodynamic or anatomic constraints), leaving one septum still not invaded at this early step. Second, common residual injuries (interstitial syndrome, consolidations, effusions) are present at the step of an SBT (unlike in patients of the BLUE protocol). This affects the functional lung volume, and it is known that in patients undergoing SBT, WIPO can appear earlier than in patients with usual hydrostatic oedema for the same values of fluid excess [6, 7].

Although it is small and hypotheses-generating, our study has potential clinical implications. First, it is now clear that WIPO is a common cause of weaning failure. Second, it is a cause for which treatment might be easy and efficient to prompt extubation. Third, the invasiveness of the reference diagnosis, the pulmonary artery catheter, is less and less acceptable today at the time of extubation, so that clinicians are looking for validated alternatives. Fourth, lung ultrasound is an easy-to-learn technique, which is today well established and more and more used at the bedside. Finally, the method we describe for WIPO diagnosis, which only consists in counting B-lines on four chest wall points, is non-invasive, costless and easy to perform.

Our study has some limitations. First and most importantly, we did not use the pulmonary artery catheter to diagnose WIPO. Nevertheless, using such an invasive technique while some alternatives have been validated would be hardly acceptable today. The same experts' opinion diagnosis has been already used by other studies about WIPO [21–23]. Moreover, the experts made the

diagnosis by taking into account several criteria, which have all been established as reliable diagnostic methods compared to the pulmonary artery catheter [6, 7]. Second, this was a single-centre study with a relatively small number of patients and no validation cohort. In particular, the incidence of weaning failure was high, likely because of the severity of illness of our patients. Note that a recent study with 283 patients shows similar rates [21]. Also, the confidence intervals of sensitivity, specificity and predictive values were wide, suggesting that our results should be confirmed. Third, in case of disagreement between experts in terms of the diagnosis of WIPO, we did not plan to ask for a third expert, which may have resolved some cases. This occurred only in one case in the present study. Fourth, we tested only SBT performed on T tubes, while weaning with pressure support is less challenging for the heart [24]; this issue should not alter the ability of LUCI to be used to diagnose WIPO. Finally, whether diagnosing WIPO with LUCI could lead to reduction of mechanical ventilation duration warrants further studies.

In conclusion, our study shows that an increase in the number of B-lines  $\geq 6$  on four anterior points during SBT provided the best accuracy for diagnosing WIPO with lung ultrasound. We suggest calling this sign the WIPO profile. These encouraging results must be confirmed by larger series, so that LUCI may empower the non-invasive monitoring tools, including biochemical indices, for the diagnosis of this common problem.

#### Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s00134-019-05573-6>) contains supplementary material, which is available to authorized users.

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#### Author contributions

XM and JLT conceived and designed the study; AF and MG recruited the patients and collected the data; DL and GM established the lung ultrasound protocol, trained and supervised AF and MG for lung ultrasound, and gave them the technical basis for lung ultrasound data acquisition; DL and GM analysed the lung ultrasound data. AF, JLT and XM analysed and interpreted the other data; AF and XM drafted the report and all authors contributed to review it. All authors approved the final version.

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#### Compliance with ethical standards

#### Conflicts of interest

Drs. Alexis Ferré, Max Guillot, Daniel Lichtenstein and Gilbert Mezière have no potential conflict of interest to declare. Profs. Xavier Monnet and Jean-Louis

Teboul are members of the Medical Advisory Board of Pulsion Medical Systems, part of Getinge.

#### Ethical approval

Approved by the institutional review board of Comité Pour la Protection des Personnes Ile-de-France 7 ID2011A017014.

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#### References

- Thille AW, Richard J-CM, Brochard L (2013) The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 187:1294–1302. <https://doi.org/10.1164/rccm.201208-1523CI>
- Routsi C, Stanopoulos I, Zakyntinos E et al (2010) Nitroglycerin can facilitate weaning of difficult-to-wean chronic obstructive pulmonary disease patients: a prospective interventional non-randomized study. *Crit Care* 14:R204. <https://doi.org/10.1186/cc9326>
- Lemaire F, Teboul JL, Cinotti L et al (1988) Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. *Anesthesiology* 69:171–179
- Teboul J-L (2014) Weaning-induced cardiac dysfunction: where are we today? *Intensive Care Med* 40:1069–1079. <https://doi.org/10.1007/s00134-014-3334-4>
- Dres M, Teboul J-L, Anguel N et al (2015) Passive leg raising performed before a spontaneous breathing trial predicts weaning-induced cardiac dysfunction. *Intensive Care Med* 41:487–494. <https://doi.org/10.1007/s00134-015-3653-0>
- Anguel N, Monnet X, Osman D et al (2008) Increase in plasma protein concentration for diagnosing weaning-induced pulmonary oedema. *Intensive Care Med* 34:1231–1238. <https://doi.org/10.1007/s00134-008-1038-3>
- Dres M, Teboul J-L, Anguel N et al (2014) Extravascular lung water, B-type natriuretic peptide, and blood volume contraction enable diagnosis of weaning-induced pulmonary edema. *Crit Care Med* 42:1882–1889. <https://doi.org/10.1097/CCM.0000000000000295>
- Zapata L, Vera P, Roglan A et al (2011) B-type natriuretic peptides for prediction and diagnosis of weaning failure from cardiac origin. *Intensive Care Med* 37:477–485. <https://doi.org/10.1007/s00134-010-2101-4>
- Lamia B, Maizel J, Ochagavia A et al (2009) Echocardiographic diagnosis of pulmonary artery occlusion pressure elevation during weaning from mechanical ventilation. *Crit Care Med* 37:1696–1701. <https://doi.org/10.1097/CCM.0b013e31819f13d0>
- Lichtenstein D (1994) Ultrasound diagnosis of pulmonary edema. *Rev Im Med* 6:561–562
- Volpicelli G, Mussa A, Garofalo G et al (2006) Bedside lung ultrasound in the assessment of alveolar-interstitial syndrome. *Am J Emerg Med* 24:689–696. <https://doi.org/10.1016/j.ajem.2006.02.013>
- Lichtenstein D, Mezière G (2009) Diagnosis of cardiogenic pulmonary edema by sonography limited to the anterior lung. *Chest* 135:883–884. <https://doi.org/10.1378/chest.08-2733>
- Liteplo AS, Marill KA, Villen T et al (2009) Emergency thoracic ultrasound in the differentiation of the etiology of shortness of breath (ETUDES): sonographic B-lines and N-terminal pro-brain-type natriuretic peptide in diagnosing congestive heart failure. *Acad Emerg Med* 16:201–210. <https://doi.org/10.1111/j.1553-2712.2008.00347.x>
- Gargani L, Frassi F, Soldati G et al (2008) Ultrasound lung comets for the differential diagnosis of acute cardiogenic dyspnoea: a comparison with natriuretic peptides. *Eur J Heart Fail* 10:70–77. <https://doi.org/10.1016/j.ejheart.2007.10.009>
- Enghard P, Rademacher S, Nee J et al (2015) Simplified lung ultrasound protocol shows excellent prediction of extravascular lung water in ventilated intensive care patients. *Crit Care* 19:36. <https://doi.org/10.1186/s13054-015-0756-5>
- Boles J-M, Bion J, Connors A et al (2007) Weaning from mechanical ventilation. *Eur Respir J* 29:1033–1056. <https://doi.org/10.1183/09031936.00010206>
- Esteban A, Alía I, Tobin MJ et al (1999) Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med* 159:512–518. <https://doi.org/10.1164/ajrccm.159.2.9803106>
- Perren A, Domenighetti G, Mauri S et al (2002) Protocol-directed weaning from mechanical ventilation: clinical outcome in patients randomized for a 30-min or 120-min trial with pressure support ventilation. *Intensive Care Med* 28:1058–1063. <https://doi.org/10.1007/s00134-002-1353-z>
- Lichtenstein D, Mezière G (2008) Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. *Chest* 134:117–125. <https://doi.org/10.1378/chest.07-2800>
- Lichtenstein D, Mezière G (2011) The BLUE-points: three standardized points used in the BLUE-protocol for ultrasound assessment of the lung in acute respiratory failure. *Crit Ultrasound J* 3:109–110
- Liu J, Shen F, Teboul J-L et al (2016) Cardiac dysfunction induced by weaning from mechanical ventilation: incidence, risk factors, and effects of fluid removal. *Crit Care* 20:369. <https://doi.org/10.1186/s13054-016-1533-9>
- Caille V, Amiel J-B, Charron C et al (2010) Echocardiography: a help in the weaning process. *Crit Care* 14:R120. <https://doi.org/10.1186/cc9076>
- Grasso S, Leone A, De Michele M et al (2007) Use of N-terminal pro-brain natriuretic peptide to detect acute cardiac dysfunction during weaning failure in difficult-to-wean patients with chronic obstructive pulmonary disease. *Crit Care Med* 35:96–105. <https://doi.org/10.1097/01.CCM.0000250391.89780.64>
- Cabello B, Thille AW, Roche-Campo F et al (2010) Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. *Intensive Care Med* 36:1171–1179. <https://doi.org/10.1007/s00134-010-1870-0>
- Dres M, Teboul J-L, Monnet X (2014) Weaning the cardiac patient from mechanical ventilation. *Curr Opin Crit Care* 20:493–498. <https://doi.org/10.1097/MCC.0000000000000131>
- Chien J-Y, Lin M-S, Huang Y-CT et al (2008) Changes in B-type natriuretic peptide improve weaning outcome predicted by spontaneous breathing trial. *Crit Care Med* 36:1421–1426. <https://doi.org/10.1097/CCM.0b013e31816f49ac>
- Figueras J, Weil MH (1978) Blood volume prior to and following treatment of acute cardiogenic pulmonary edema. *Circulation* 57:349–355
- de Meirelles Almeida CA, Nedel WL, Morais VD et al (2016) Diastolic dysfunction as a predictor of weaning failure: a systematic review and meta-analysis. *J Crit Care* 34:135–141. <https://doi.org/10.1016/j.jccr.2016.03.007>
- Dres M, Teboul J-L, Guerin L et al (2014) Transpulmonary thermodilution enables to detect small short-term changes in extravascular lung water induced by a bronchoalveolar lavage. *Crit Care Med* 42:1869–1873. <https://doi.org/10.1097/CCM.0000000000000341>
- Monnet X, Teboul J-L (2017) Transpulmonary thermodilution: advantages and limits. *Crit Care* 21:147. <https://doi.org/10.1186/s13054-017-1739-5>
- Soummer A, Perbet S, Brisson H et al (2012) Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress. *Crit Care Med* 40:2064–2072. <https://doi.org/10.1097/CCM.0b013e31824e68ae>
- Silva S, Ait Aissa D, Cocquet P et al (2017) Combined thoracic ultrasound assessment during a successful weaning trial predicts postextubation distress. *Anesthesiology* 127:666–674. <https://doi.org/10.1097/ALN.0000000000001773>
- Gargani L, Volpicelli G (2014) How I do it: lung ultrasound. *Cardiovasc Ultrasound* 12:25. <https://doi.org/10.1186/1476-7120-12-25>
- Lichtenstein D (2017) Novel approaches to ultrasonography of the lung and pleural space: where are we now? *Breathe (Sheff)* 13:100–111. <https://doi.org/10.1183/20734735.004717>